546-D GAO/HRD PEMD 88-12BR

United States General Accounting Office

GAO

COMPLETED
23

Briefing Report to the Chairman, Subcommittee on Health and the Environment, Committee on Energy and Commerce, House of Representatives

January 1988

CANCER TREATMENT 1975-85

The Use of Breakthrough Treatments for Seven Types of Cancer

ORIGINAL

GAO/PEMD-88-12BR

G M Jim

GAO

United States
General Accounting Office
Washington, D.C. 20548

Program Evaluation and
Methodology Division

B-226468

January 25, 1988

The Honorable Henry A. Waxman
Chairman, Subcommittee on Health and
the Environment
Committee on Energy and Commerce
House of Representatives

Dear Mr. Chairman:

One reason often given for why cancer survival rates have not improved dramatically in recent years is that many patients do not receive state-of-the-art therapies. The view that the latest therapies are not widely applied has been expressed by many experts in cancer-patient treatment, including those at the National Cancer Institute (NCI). In your June 2, 1987, letter, you asked us to determine whether this view is true and, if so, the magnitude of the problem. This briefing report is a preliminary study focusing on the one issue of the percentage of patients who were clinically eligible to receive "breakthrough" treatments but did not. The report contains seven sections, each of which examines the usage patterns for a specific "breakthrough." Our three-step methodology is described below. We intend to provide you later this year with a full report on all the issues you asked us to examine.

METHODOLOGY

The Selection of Treatment Breakthroughs

Since much has changed in the treatment of cancer patients in recent decades, our first concern was which state-of-the-art treatments to include in our study. A representative sample of new treatments would have been difficult, if not impossible, to develop. Therefore, we asked NCI to provide us with a list of all breakthroughs in cancer treatment that met the following criteria:

-- they occurred by 1982 (so as to allow us to determine patterns of use with the available data on treatment),

-- they had been proven to increase patients' survival in a large randomized clinical trial, and

-- they were relevant for an identifiable group of cancer patients.

NCI forwarded a list of treatment advances that was based on these criteria. We excluded the treatment of osteosarcoma and soft tissue sarcoma, because there were too few patients with these types of cancer to allow for reliable analyses. We discuss the seven remaining treatments in this report: adjuvant chemotherapy for breast cancer, adjuvant chemotherapy for colon cancer, adjuvant radiation therapy for rectum cancer, chemotherapy for small-cell lung cancer, chemotherapy for testicular cancer, chemotherapy for Hodgkin's disease, and chemotherapy for non-Hodgkin's lymphoma.

The Selection of Patients

Few, if any, treatments are appropriate for all patients suffering from any one type of cancer. As a disease progresses, the appropriate treatment for it typically changes. Given that our goal was to determine the percentage of patients who did not receive specific treatments, it was clear that the common denominator should be not "all patients" but, rather, "all patients for whom the treatments would have been appropriate."

Since determining the appropriateness of a specific treatment for a class of patients requires clinical expertise, we again asked NCI for assistance. NCI defined the types of patients who should have received each of the seven treatment breakthroughs (for example, adjuvant chemotherapy is appropriate for premenopausal women with breast cancer whose tumors are smaller than 5 centimeters and who have positive lymph nodes). We excluded patients from the analyses for whom it was not clear whether a treatment should definitely have been given. The types of patients included in our analyses made up a group that, in the opinion of NCI, could have benefited from the treatment advances for each of their respective cancers.

Data Source and Analysis Plan

Once we had a list of treatments and had identified the types of patients for whom each was appropriate, the analysis was straightforward. We used NCI's criteria to select patients from all the patients in the Surveillance, Epidemiology, and End Results (SEER) data base. NCI collects the SEER data from population-based registries that cover areas representing approximately 12 percent of the U.S. population. The SEER population is not a probability sample of the country, but it is believed to represent overall cancer patterns.

Having selected the patients from the SEER data, we examined the percentage of those patients who did not receive the treatments in question. We based our decision to focus on the "nonreceivers" on the fact that the SEER data on treatment are not sufficiently precise to inform us as to whether state-of-the-art therapy was actually given. For example, SEER data will tell whether or not a patient received chemotherapy but do not indicate the exact type of chemotherapeutic regimen administered, which might consist of a new combination of three specific drugs. As a result, we can be sure that patients who did not receive chemotherapy did not receive the breakthrough treatment in chemotherapy, but we cannot be sure that patients whose treatments included chemotherapy actually received the breakthrough treatment.

In SEER, treatments are covered in one of three ways: given, not given, and planned. The data in SEER are drawn from the hospital records of the individual patients and indicate the first course of treatment. In our analyses of these data, we combined the categories "given" and "planned." As a result, our findings on "the percentage of patients who did not receive specific therapies" may exclude patients for whom the treatments were planned yet never provided.

If there is a limitation in the data, it is that SEER data are drawn exclusively from hospital records. As a result, treatments given outside of hospitals following patients' hospital stays may be missed. This is less serious a problem because SEER does collect data on the first course of treatment, even if it is given outside the hospital. However, treatments planned while patients are in the hospital and not recorded in patient case records, would be missed.

SUMMARY OF FINDINGS

As one looks across the seven sections that follow, a considerable variation in usage patterns becomes clear. The use of some treatments (for example, radiation therapy for rectum cancer) seems to be increasing, while the use of others (for example, chemotherapy for colon cancer) seems to be waning. Why treatment usage rises and falls and whether these trends will continue are questions beyond our present scope. As a result, we cannot be sure whether the obstacles to a more widespread application lie with physicians or patients or both or neither. What this report does show, however, is that a considerable group of patients among those who had the seven cancers we examined--20 percent of those with Hodgkin's disease, 25 percent of those with one type of lung cancer, 60 percent of those with rectum cancer, 94 percent of colon cancer patients--did not receive what NCI considers state-of-the-art treatments. This is especially troubling in that all these treatments have been proven to extend patients' survival in controlled experiments, many of which were concluded 10 or more years ago.

As you requested, we did not send this report to NCI for comment prior to publication. As we arranged with your office, unless you announce the contents of this report earlier, we plan no further distribution of it until 30 days from the date of the report. At that time, we will send copies to the secretary of the Department of Health and Human Services, the director of the National Institutes of Health, and the director of the National Cancer Institute. We will also make copies available to interested organizations, as appropriate, and to others upon request.

Sincerely yours,

Eleanor Chelimsky
Director

BLANK PAGE

C O N T E N T S

		Page
SECTION		
1	ADJUVANT CHEMOTHERAPY FOR BREAST CANCER	8
2	ADJUVANT CHEMOTHERAPY FOR COLON CANCER	10
3	ADJUVANT RADIATION THERAPY FOR RECTUM CANCER	12
4	CHEMOTHERAPY FOR SMALL-CELL LUNG CANCER	14
5	CHEMOTHERAPY FOR TESTICULAR CANCER	16
6	CHEMOTHERAPY FOR HODGKIN'S DISEASE	18
7	CHEMOTHERAPY FOR NON-HODGKIN'S LYMPHOMA	20
FIGURE		
1.1	Breast Cancer Patients Who Did Not Receive Adjuvant Chemotherapy As First Course of Treatment 1975-85	8
1.2	Treatment of Breast Cancer, 1975-85	9
2.1	Colon Cancer Patients Who Did Not Receive Adjuvant Chemotherapy As First Course of Treatment 1975-85	10
2.2	Treatment of Colon Cancer, 1975-85	11
3.1	Rectum Cancer Patients Who Did Not Receive Adjuvant Radiation Therapy As First Course of Treatment 1975-85	12
3.2	Treatment of Rectum Cancer, 1975-85	13
4.1	Small-Cell Lung Cancer Patients Who Did Not Receive Chemotherapy as First Course of Treatment 1975-85	14
4.2	Treatment of Small-Cell Lung Cancer, 1975-85	15
5.1	Nonseminoma Testis Cancer Patients Who Did Not Receive Chemotherapy As First Course of Treatment 1975-85	16

5.2 Treatment of Nonseminoma Testis Cancer, 1975-85 17

6.1 Hodgkin's Disease Patients Who Did Not Receive Chemotherapy As First Course of Treatment 1977-85 18

6.2 Treatment of Hodgkin's Disease, 1977-85 19

7.1 Non-Hodgkin's Lymphoma Patients Who Did Not Receive Chemotherapy As First Course of Treatment 1977-85 20

7.2 Treatment of Non-Hodgkin's Lymphoma, 1977-85 21

ABBREVIATIONS

HD Hodgkin's disease

NCI National Cancer Institute

NHL Non-Hodgkin's lymphoma

SEER Surveillance, Epidemiology, and End Results

SECTION 1

ADJUVANT CHEMOTHERAPY FOR BREAST CANCER

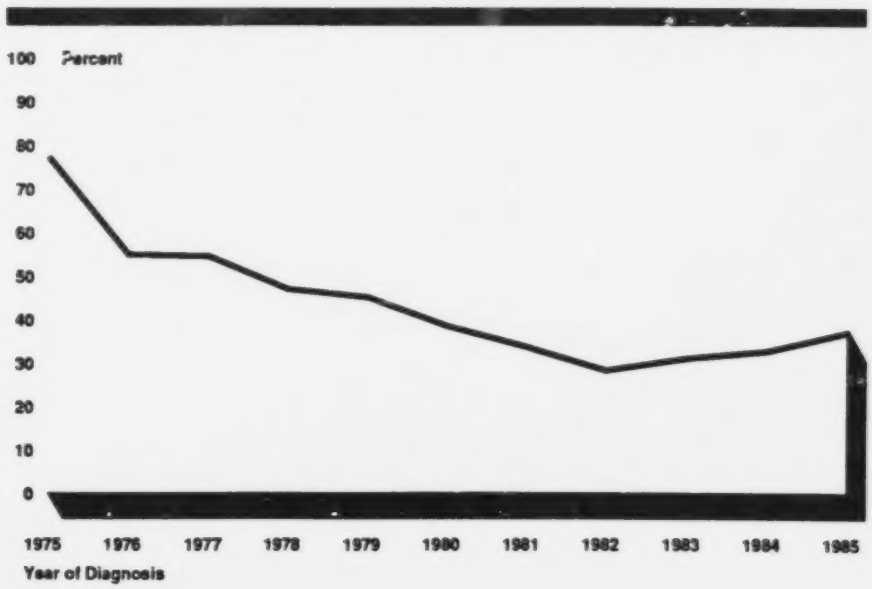
While it is has been shown that surgery is a highly effective treatment for most localized breast cancers, the effectiveness of surgery alone for regional disease (that is, where the lymph nodes under the arm have become involved) remains open to debate. In the mid-1970's, however, at least one part of that debate was resolved when clinical trials proved that surgery alone is not as effective in extending the survival of premenopausal women with breast cancer as surgery followed by combination chemotherapy. NCI identified the development of multidrug combinations to be given as adjuvants to surgery as a significant breakthrough in cancer-patient treatment.

RELEVANT POPULATION

Chemotherapy was judged to be most relevant for premenopausal women whose tumors were smaller than 5 centimeters when diagnosed, had spread to regional lymph nodes but not to distant organs, and were classified as adenocarcinoma or duct adenocarcinoma. In addition, as the term "adjuvant" implies, the chemotherapy had the greatest relevance when "added to" surgery.

These criteria, using an age cutoff of 50 years and younger at the time of diagnosis as a surrogate for premenopause, yielded

Figure 1.1: Breast Cancer Patients Who Did Not Receive Adjuvant Chemotherapy as First Course of Treatment 1975-85



BEST COPY AVAILABLE

a population of 5,488 breast cancer patients of all breast cancer cases in the SEER data in the period between 1975 and 1985.

DISCUSSION

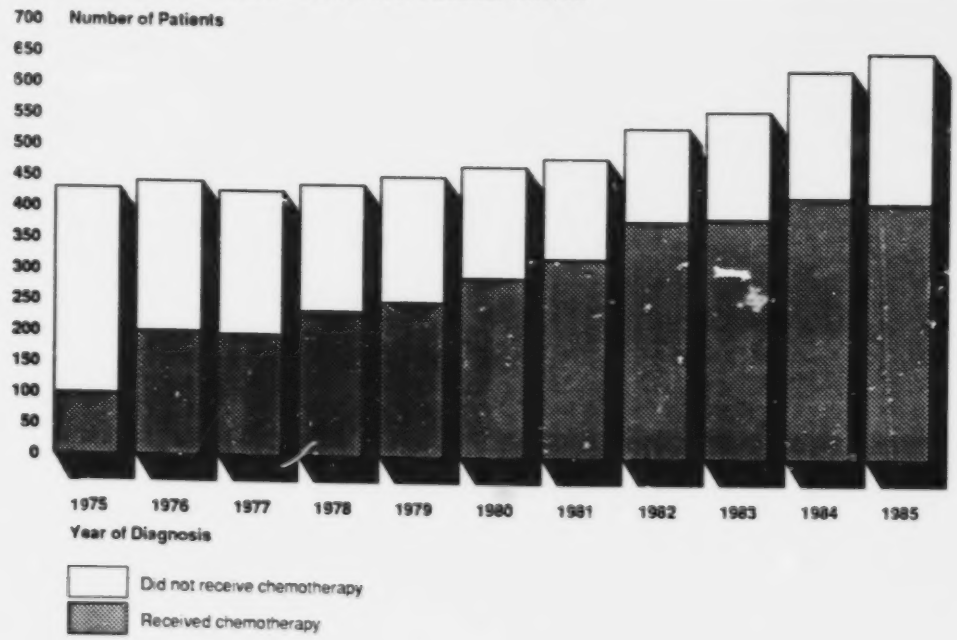
As can be seen from figure 1.1, there was a steady decrease in the percentage of breast cancer patients who failed to receive adjuvant chemotherapy from 1975 to 1982, and there has been a slight increase in that percentage since 1982. Perhaps the two most significant aspects of the data are that

-- there has been an approximately threefold increase in the administration of chemotherapy following surgery for breast cancer among premenopausal women (22.9 percent in 1975 to 63.1 percent in 1985) and

-- more than one third (36.9 percent) of those women still do not get adjuvant chemotherapy, approximately 10 years after clinical trials proved that adjuvant chemotherapy improves the survival chances of young women with regional breast cancer.

Figure 1.2 indicates the breast cancer patients in our analysis by year of diagnosis and whether they did or did not receive chemotherapy following surgery.

Figure 1.2: Treatment of Breast Cancer Patients 1975-85



BEST COPY AVAILABLE

SECTION 2

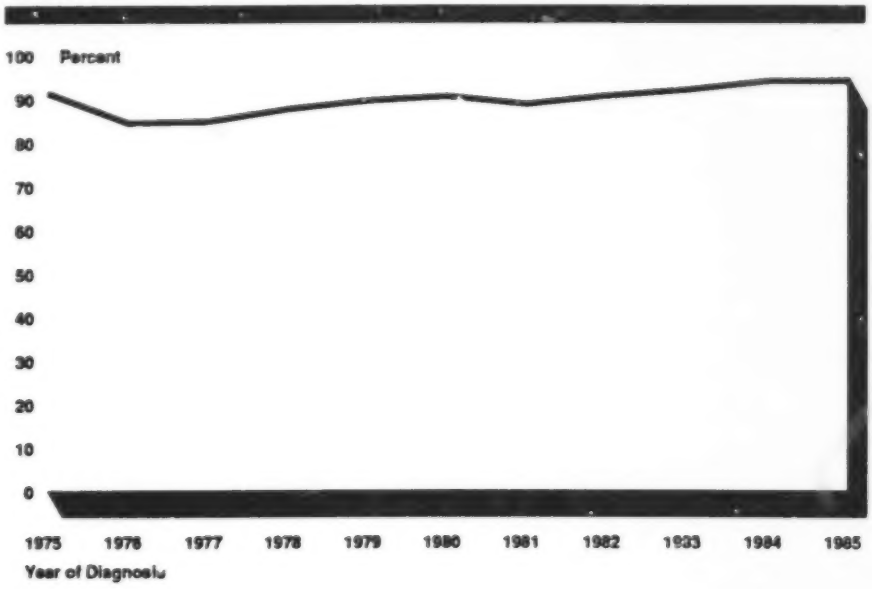
ADJUVANT CHEMOTHERAPY FOR COLON CANCER

As with breast cancer, surgery is an effective form of treatment for early colon cancer. Nevertheless, colon cancer recurs in approximately half the patients treated with surgery for this disease. In order to reduce the recurrence, various therapies have been tried as adjuvants to surgery. According to NCI, one that has improved patients' survival is high-dose 5-Fluorouracil (5-FU). The administration of chemotherapy to colon cancer patients who have undergone surgery was another of the treatment advances NCI identified for us as significant.

RELEVANT POPULATION

Chemotherapy was judged to be valuable for colon cancer patients whose tumors had spread through the serosa or to the mesentary, as well as for patients with more limited tumor extension if their regional lymph nodes were involved. In addition, the patients were most likely to benefit if their distant organs or lymph nodes had not yet become involved and if they were treated with chemotherapy in addition to surgery.

Figure 2.1: Colon Cancer Patients Who Did Not Receive Adjuvant Chemotherapy as First Course of Treatment 1975-85



BEST COPY AVAILABLE

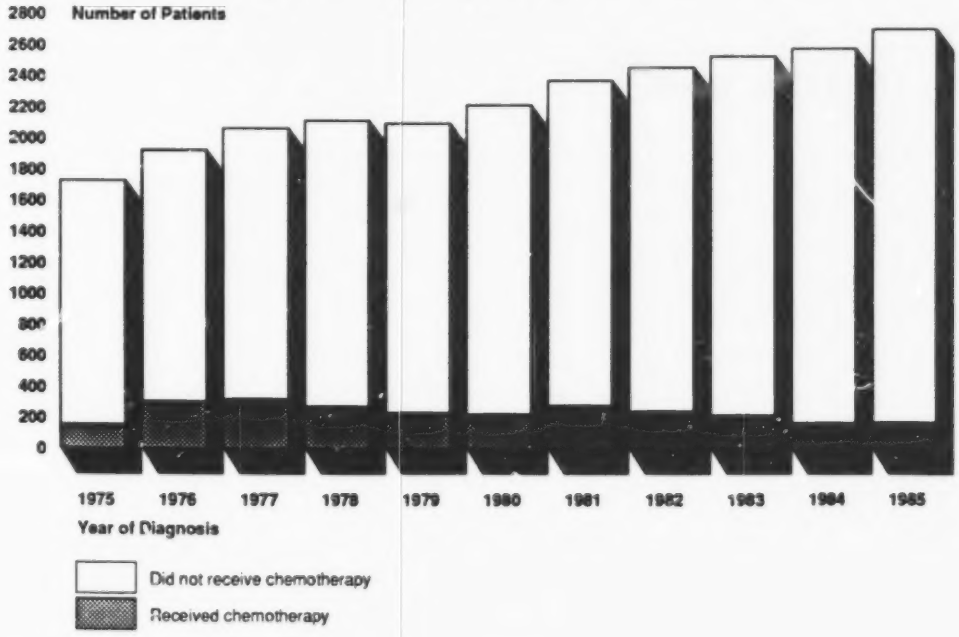
These criteria yielded a population of 24,651 colon cancer patients of all colon cancer cases in the SEER data base in the period between 1975 and 1985.

DISCUSSION

Of the seven treatment advances we examined, adjuvant chemotherapy for colon cancer evidenced by far the least use throughout the 11-year period under consideration. As figure 2.1 shows, in the years following 1981 more than 90 percent of patients did not receive any type of chemotherapy as part of their treatments. By 1985, this figure had risen to 94 percent of all the colon patients we included in our analysis. Unless there was a change after 1985, it is clear that this treatment has not been adopted into general clinical practice.

Figure 2.2 indicates the colon cancer patients in our analysis by year of diagnosis and whether they did or did not receive chemotherapy following surgery.

Figure 2.2: Treatment of Colon Cancer Patients 1975-85



BEST COPY AVAILABLE

SECTION 3

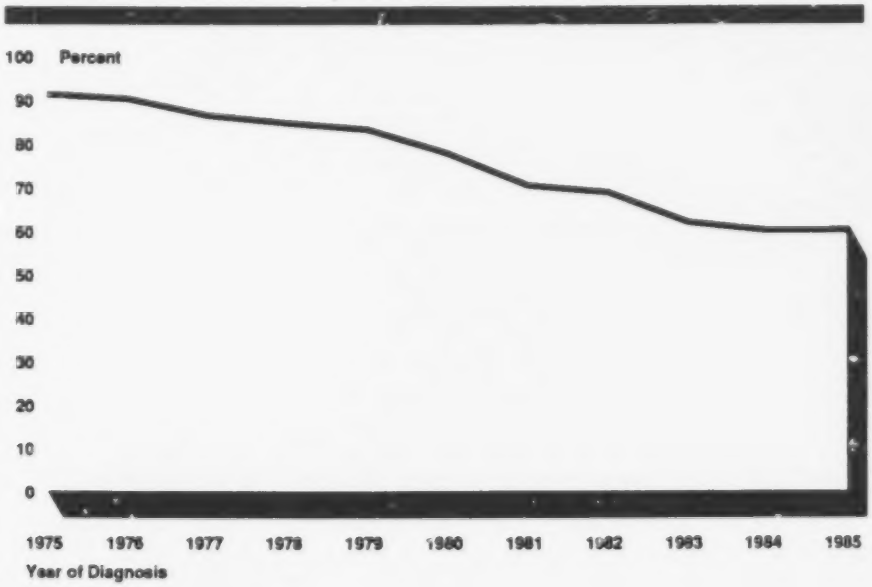
ADJUVANT RADIATION THERAPY FOR RECTUM CANCER

Since rectum cancer is similar to colon cancer in many ways, the two are often combined in discussions of the origin of cancer and its epidemiology. The two cancers also share the characteristic of being curable with surgery alone while they are in the earliest stages of development. One significant difference between colon and rectum cancers, however, is that only the latter seem to respond well to radiation therapy. Clinical trials completed in the late 1970's showed a definite advantage in survival for rectum cancer patients who were irradiated in addition to being surgically operated on, compared with a matched group of patients who received only surgery. The use of radiation therapy in combination with surgery for treating rectum cancer patients was one of the significant advances NCI recommended to us.

RELEVANT POPULATION

The criteria that qualify a rectum cancer patient for radiation therapy are exactly those that qualify colon cancer patients for high-dose 5-FU. These criteria yielded a population of 9,057 rectum cancer patients of all rectum cancer patients in the SEER data between 1975 and 1985.

Figure 3.1: Rectum Cancer Patients Who Did Not Recieve Adjuvant Radiation Therapy as First Course of Treatment 1975-85



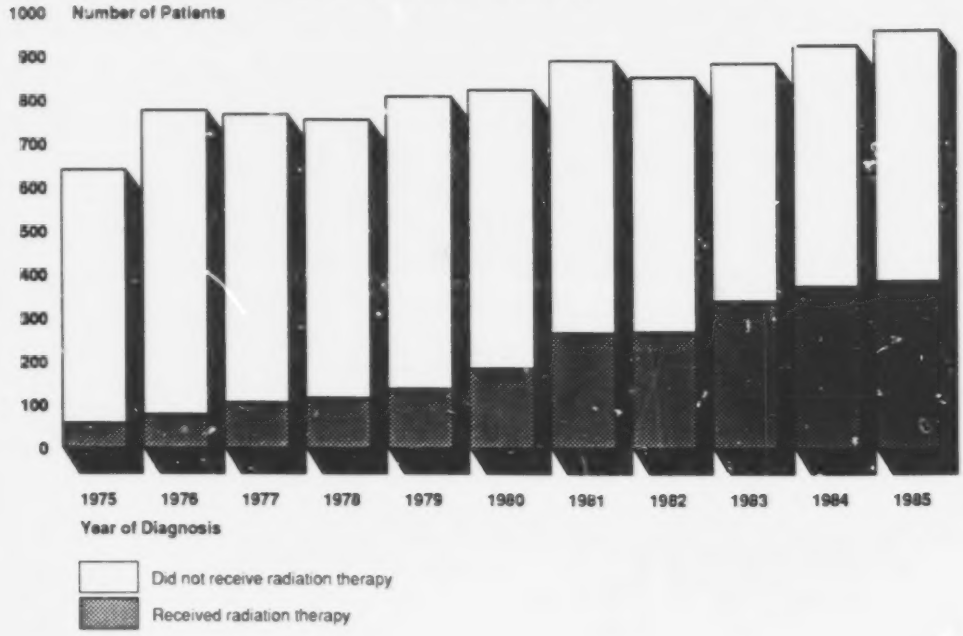
BEST COPY AVAILABLE

DISCUSSION

As can be seen from figures 3.1 and 2.1, the pattern of the use of adjuvant radiation therapy in the treatment of rectum cancer was dramatically different from that for adjuvant chemotherapy for colon cancer. Unlike the colon cancer patients, the percentage of rectum cancer patients not being given the treatment advance decreased steadily after 1975. There was a more than fourfold increase in the relative use of radiation therapy for rectum cancer during the 11-year period we examined. Still, in 1985, 60 percent of the patients who might have benefited from the radiation therapy were not receiving it.

Figure 3.2 indicates the rectum cancer patients in our analysis by year of diagnosis and whether they did or did not receive radiation therapy in addition to surgery.

Figure 3.2: Treatment of Rectum Cancer Patients 1975-85



BEST COPY AVAILABLE

SECTION 4

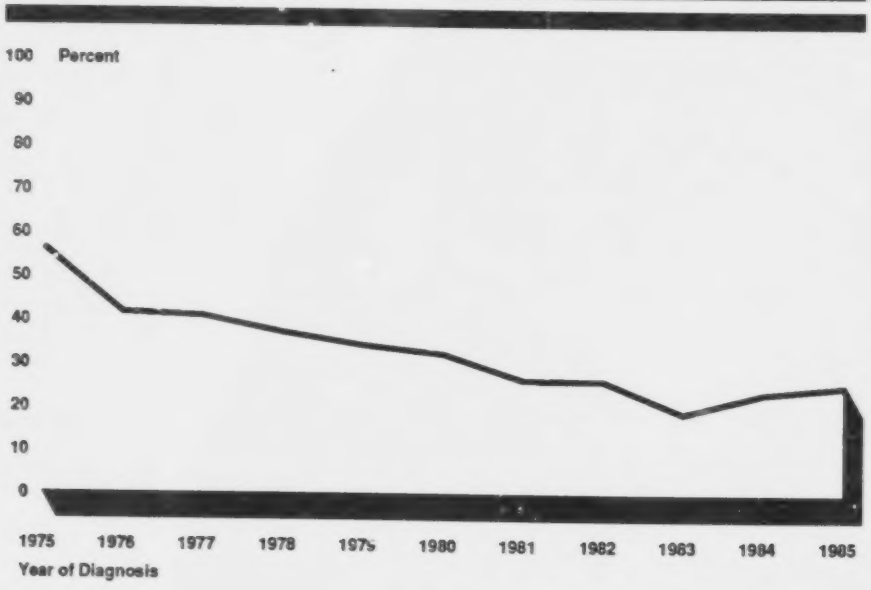
CHEMOTHERAPY FOR SMALL-CELL LUNG CANCER

Lung cancer is responsible for more deaths every year than any other cancer. The incidence of the disease is high, and the prognosis is poor. Of the four most prevalent types of lung cancer, small-cell carcinoma has typically offered the poorest prognosis to its victims. In recent years, however, a multidrug regimen has been tested and proven effective not only in extending the lives of small-cell cancer victims but even in actually curing some of them. NCI identified the ability to cure some lung cancer patients with chemotherapy as another important treatment advance.

RELEVANT POPULATION

Although nearly every patient with small-cell carcinoma of the lung may benefit from chemotherapy, the effectiveness of the treatment decreases in the later stages of the disease. For this reason, we restricted our analysis to patients with "limited" small-cell cancer, a class that generally includes patients whose tumors were confined to the lungs and did not extend beyond the regional lymph nodes. This criterion yielded a population of 3,801 small-cell lung cancer patients of all patients diagnosed in the SEER data between 1975 and 1985.

Figure 4.1: Small-cell Lung Cancer Patients Who Did Not Receive Chemotherapy 1975-85



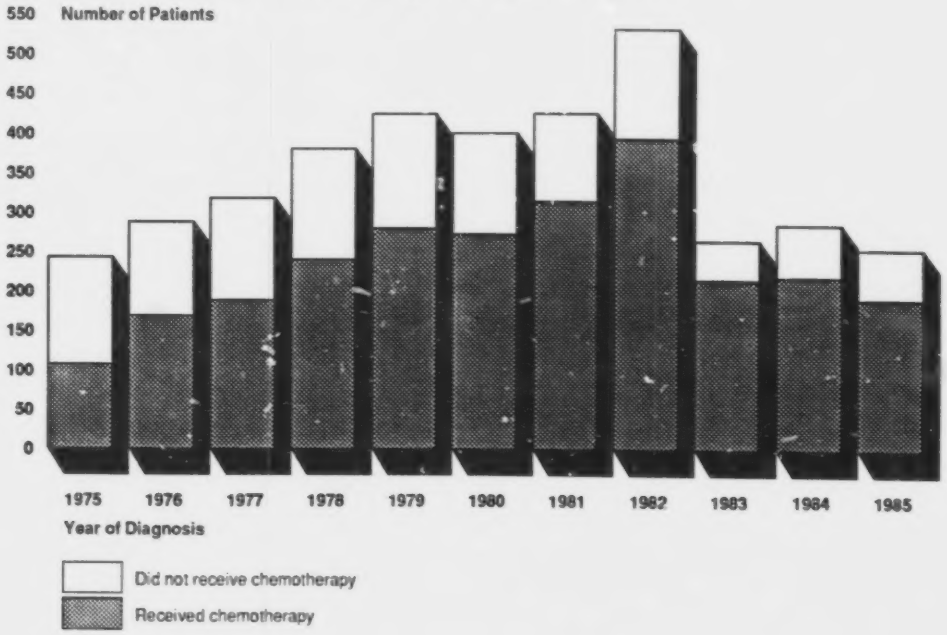
BEST COPY AVAILABLE

DISCUSSION

The percentage of patients with limited small-cell lung cancer not receiving chemotherapy was low relative to the treatment patterns for many of the other cancers we examined. As figure 4.1 shows, approximately 56 percent of the patients diagnosed in 1975 did not receive chemotherapy and this figure dropped to 25 percent by 1985. Although the SEER data do not allow us to determine the types of chemotherapy that were given to patients, our findings clearly show that some form of chemotherapy has become a relatively standard part of the management of patients with limited small-cell cancer of the lung.

Figure 4.2 indicates the lung cancer patients in our analysis by year of diagnosis and whether they did or did not receive chemotherapy. There is a decline in the number of small-cell cancer patients in our sample beginning in 1983. This decline occurs after a change in the coding of SEER and represents an increase in the percentage of cases whose extent of disease is identified as unknown and not a decline in the total number of cases.

Figure 4.2: Treatment of Small-Cell Lung Cancer Patients 1975-85



BEST COPY AVAILABLE

SECTION 5

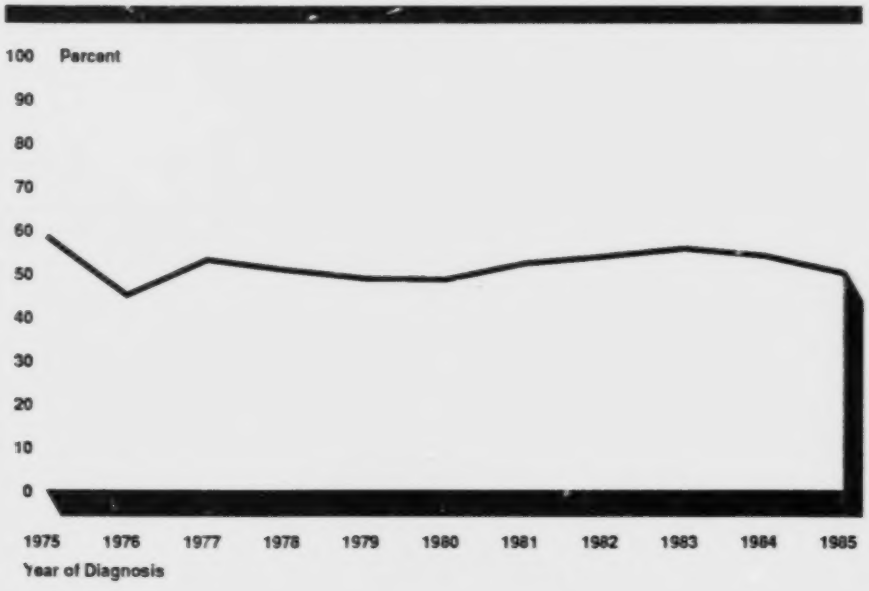
CHEMOTHERAPY FOR TESTICULAR CANCER

Although a relatively rare disease, cancer of the testis is one of the major causes of cancer-related deaths among men younger than 40. The many different types of testicular cancer are generally classified as either seminomas or nonseminomas. The distinction is made because it has been known for some time that seminomas are radiosensitive and, therefore, can be cured with radiation therapy, while the same is not true for other forms of testicular cancer. In 1977, however, it was demonstrated that the nonseminomas are highly responsive to a multidrug combination and later studies showed that long-term survival can be achieved for even advanced cases of this form of cancer.

RELEVANT POPULATION

We considered all patients with nonseminoma testis cancers in the SEER data between 1975 and 1985 as possible candidates for chemotherapy. Using this criterion yielded a population of 2,185 nonseminoma testis cancer patients.

Figure 5.1: Nonseminoma Testis Cancer Patients Who Did Not Receive Chemotherapy as First Course of Treatment 1975-85



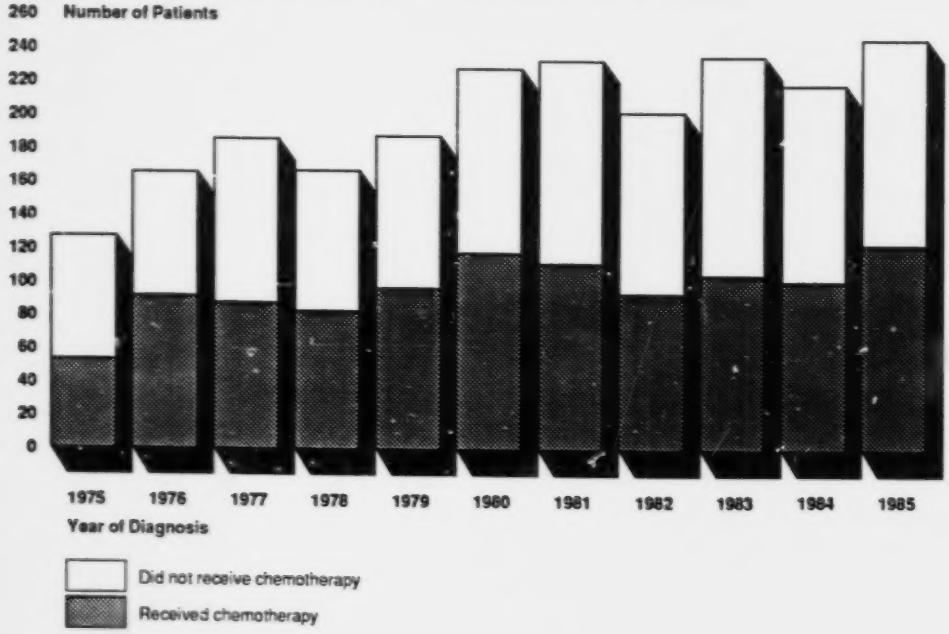
BEST COPY AVAILABLE

DISCUSSION

Figure 5.1 shows that not much changed in the usage of chemotherapy for nonseminoma testis cancer: 58 percent of the patients did not receive chemotherapy in 1975, 50 percent in 1985. There is a problem, however, in the interpretation of figure 5.1. NCI deferred on specifying a group of patients (other than the small number with the widely spread disease) that should necessarily have had chemotherapy as part of their initial treatment. Despite the fact that the effectiveness of chemotherapy decreases somewhat in the later stages of the disease, according to NCI, the therapy is so effective that a conservative approach to patient management may be appropriate for some patients. That is, since chemotherapy is effective even with advanced forms of testis cancer, the side effects associated with chemotherapy might appropriately point to a treatment plan in which surgery is followed by careful monitoring of some patients to see whether chemotherapy is necessary.

Figure 5.2 indicates the nonseminoma testis cancer patients in our analysis, by year of diagnosis and whether they did or did not receive chemotherapy.

Figure 5.2: Treatment of Nonseminoma Testis Cancer Patients 1975-85



BEST COPY AVAILABLE

SECTION 6

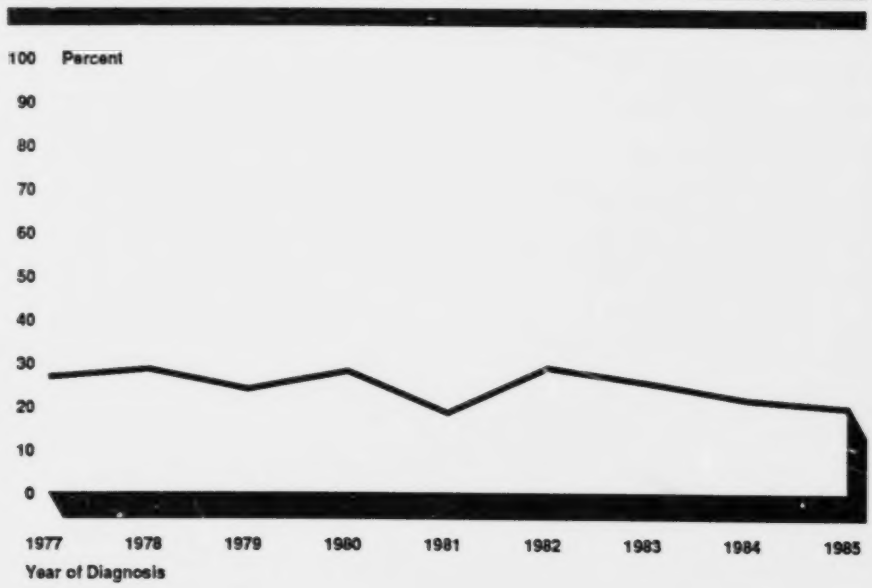
CHEMOTHERAPY FOR HODGKIN'S DISEASE

Hodgkin's disease (HD) is one of two major types of lymphomas, or cancers of the lymphatic system. Although patients with lymphomas sometimes develop tumors in specific areas that can be surgically removed, surgery alone is not an effective treatment for many forms of lymphoma. It has been known for some time that radiation therapy is effective in curing many patients suffering from HD, especially patients with the early stages of the disease. Cure rates are substantial, even for patients whose cancers have advanced to lymph nodes on both sides of the diaphragm (Stage III HD). Before the 1970's, one problem in the management of HD patients was that there was no curative therapy for cases in which the cancer had spread to organs outside the lymphatic system. In the early 1970's, however, it was shown that one combination of drugs could cure even advanced HD. The use of chemotherapy, either alone or in combination with radiation therapy, to treat advanced HD was one of the advances NCI considered a significant breakthrough.

RELEVANT POPULATION

Chemotherapy was judged to be valuable for any HD patient with Stage IIIb or Stage IV cancer. Because of problems in identifying Stage IIIb patients in a comparable fashion for all years, however, our analysis included only those patients with Stage IV HD. This group consisted of patients whose cancers had

Figure 6.1: Hodgkin's Disease Patients Who Did Not Receive Chemotherapy as First Course of Treatment 1977-85



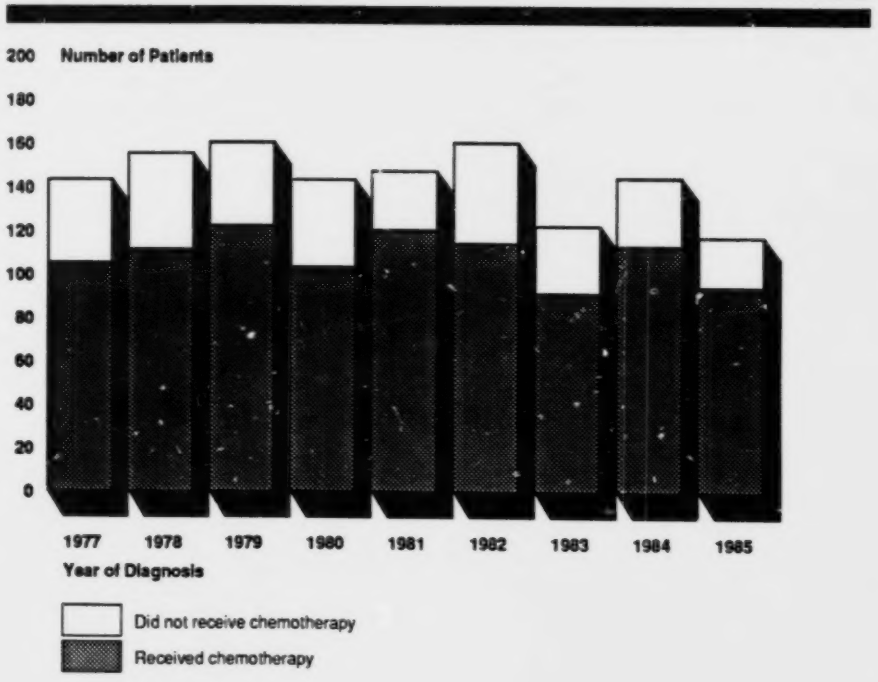
spread to extranodal sites--for example, the stomach, liver, or lungs--and included 1,291 patients in the SEER data in the period 1977-85. For both HD and non-Hodgkin's lymphoma, we also excluded patients diagnosed prior to 1977, because the SEER coding for 1975 and 1976 does not permit comparable selection across years.

DISCUSSION

An article announcing the benefits of combination chemotherapy for advanced HD was published in 1970. By 1977, 73 percent of the cases in SEER received some form of chemotherapy. This climbed only slightly over the ensuing years, so that by 1985, 80 percent were being given chemotherapy. From these percentages, it is clear that chemotherapy has been incorporated into the general clinical management of most HD patients. However, it is also true that at least 18 percent of eligible patients diagnosed in any year following 1977 did not receive chemotherapy.

Figure 6.2 indicates the Hodgkin's disease patients in our analysis by year of diagnosis and whether they did or did not receive chemotherapy.

Figure 6.2: Treatment of Hodgkin's Disease Patients 1977-85



BEST COPY AVAILABLE

SECTION 7

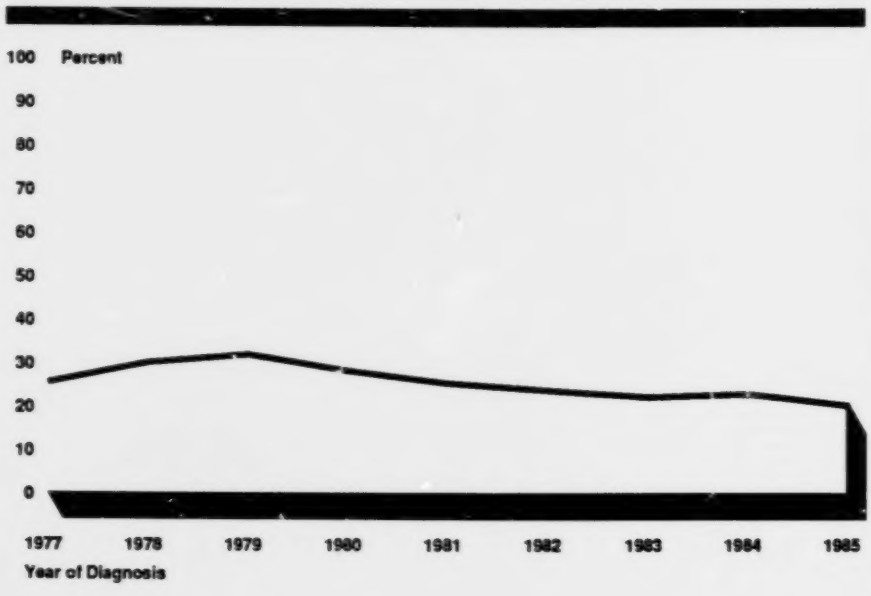
CHEMOTHERAPY FOR NON-HODGKIN'S LYMPHOMA

A logical outgrowth of the success achieved by using multidrug regimens to treat Hodgkin's disease was to attempt similar drug combinations to treat other types of lymphomas. By the late 1970's, it was clear that certain combinations of drugs are effective in treating certain kinds of lymphomas. Ironically, the drugs are the most effective against the more aggressive forms of the class of diseases known collectively as non-Hodgkin's lymphoma (NHL) and have cured many patients suffering from these forms of NHL that were necessarily fatal before the drug treatment was known. The use of chemotherapy to treat the aggressive NHLs was a treatment advance recommended to us by NCI.

RELEVANT POPULATION

Any patient with a diffuse form of NHL of intermediate or high grade whose cancer had spread to sites outside the lymphatic system was judged to be an appropriate candidate for chemotherapy. These criteria yielded a population of 3,377 NHL cases in the SEER data in the period 1977-85. We could not include patients diagnosed in 1975 and 1976, because the coding scheme for SEER does not permit a selection in these years that is based on extension to the lymphatic system.

Figure 7.1: Non-Hodgkin's Lymphoma Patients Who Did Not Receive Chemotherapy as First Course of Treatment 1977-85

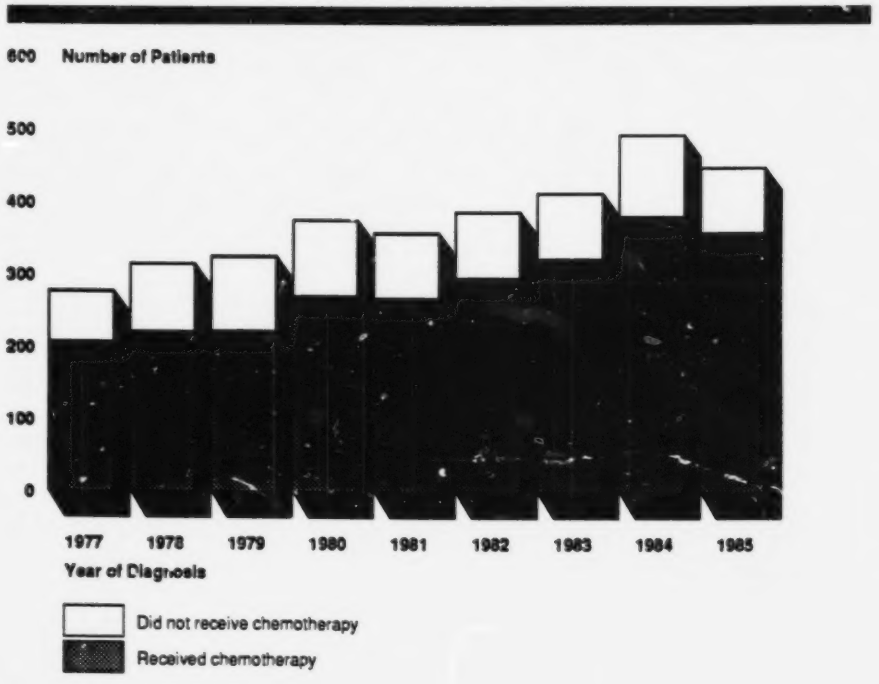


DISCUSSION

As figure 7.1 shows, there was approximately a 10-percent decline in the percentage of NHL patients not receiving chemotherapy from 1979 to 1985. By the end of the period, about one fifth (20.2 percent) of the eligible patients were still not being given chemotherapy.

Figure 7.2 indicates the non-Hodgkin's lymphoma patients in our analysis by year of diagnosis and whether they did or did not receive chemotherapy.

Figure 7.2: Treatment of Non-Hodgkin's Lymphoma Patients 1977-85



(973231)

BEST COPY AVAILABLE

Requests for copies of GAO reports should be sent to:

U.S. General Accounting Office
Post Office Box 6015
Gaithersburg, Maryland 20877

Telephone 202-275-6241

The first five copies of each report are free. Additional copies are $2.00 each.

There is a 25% discount on orders for 100 or more copies mailed to a single address.

Orders must be prepaid by cash or by check or money order made out to the Superintendent of Documents.